RISKS OF CONTRACEPTION AND PREGNANCY IN HEART DISEASE

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Heart disease is the single most common cause of maternal death in the UK,[1] with substandard care being reported in up to 40% of these deaths. Cardiologists need to be able to both advise women with heart disease of the risks of pregnancy and to give them the information they need to avoid unplanned pregnancies safely.

BACKGROUND

There is a lack of published data about contraception for women with heart disease. As a result, family planning physicians may be over-cautious, denying women appropriate contraception, thus leading to unplanned pregnancies.[2] Similarly, cardiologists may be unaware of the range of effective and safe contraceptive methods so that patients with the highest risk lesions may not have access to effective contraception and have unintended, high risk pregnancies. In extreme examples women whose cardiac risk associated with pregnancy is low have been advised to undergo termination and sterilisation.

For each contraceptive method the contraceptive efficacy and the cardiovascular risks should be considered. Likewise, for each cardiac condition, the choice of contraceptive method depends on the cardiac risks associated with the method, the level of contraceptive efficacy required (high in those for whom unplanned pregnancy may be life-threatening), and on patient choice.

The risk of pregnancy for women with heart disease depends on the specific cardiac condition and ranges from up to 50% risk of maternal death for pulmonary hypertension, to the same as the general population for minor lesions such as mild pulmonary stenosis.

In general, there is poor provision of family planning and pre-pregnancy advice for women with heart disease.[2] In particular, there is a lack of specialist services for the growing population of young women with congenital heart disease. Few cardiologists have practical knowledge of the interactions between complex heart disease, pregnancy and contraception. Advice from a multispecialty team of family planning clinicians, cardiologists and obstetricians with appropriate specialist skills should equip women with the understanding to make their own decisions about planned future pregnancies, or to adjust to the possibility of not having a pregnancy.

For all these reasons a working group of specialist cardiologists, maternal medicine physicians, obstetricians, family planning physicians and obstetric anaesthetists convened to produce guidelines and recommendations for pregnancy and contraception in heart disease (see appendix for working group members).[3] The aim of this educational article is to provide a classification of risk for cardiac lesions. For more information about contraception, pre-pregnancy assessment and antenatal management of individual cardiac lesions, please refer to more detailed publications.[3 4]

CLASSIFICATION OF RISK

The World Health Organization (WHO) classification for use of contraceptive methods (table 1) has been adapted to classify:

- the risk of different contraceptive methods for specific cardiovascular conditions
- the maternal risk of pregnancy associated with specific cardiovascular conditions.

PREGNANCY

Specialist pre-conception counselling should be available to all women with heart disease. It should begin at the time of diagnosis for women with acquired disease, and during adolescence for those with congenital heart disease. Counselling should allow women to come to terms with potential limitations on their childbearing potential, including an understanding:

- of a need for an up to date assessment before conception
- of a possible need for pre-pregnancy intervention to reduce the risk of pregnancy
- of the desirability of avoiding delaying pregnancy until their late 30s for women in whom the maternal risk will inevitably increase with age (for example, in patients with a systemic right ventricle)
- that, in some cases, pregnancy may be so high risk it is inadvisable.

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Table 1 World Health Organization (WHO) classification of risk from contraceptive use and pregnancy in cardiovascular disease

WHO class	Risk for contraceptive method by cardiac condition	Pregnancy risk by cardiac condition
WHO 1 **A**lways useable	Risk no higher than general population	Risk no higher than general population
WHO 2 **B**roadly useable	Small increased risk; advantages of method generally outweigh risks	Small increased risk of maternal mortality and morbidity
WHO 3 **C**aution in use	Risks usually outweigh advantages of method. Other methods preferable. Exceptions if: 1. Patient accepts risks and rejects alternatives 2. Risk of pregnancy very high and other methods less effective	Significant increased risk of maternal mortality and morbidity. Expert cardiac and obstetric pre-pregnancy, antenatal and postnatal care required
WHO 4 **D**o not use	Method contraindicated: represents unacceptable health risk	Pregnancy contraindicated: very high risk of maternal mortality or severe morbidity. Termination should be discussed. If pregnancy continues, care as for class 3

Pregnancy related risks are additive, so that a patient with a cardiac condition that is considered low risk (WHO 1 or 2) may move up a risk category if there are other cardiac or non-cardiac risk factors such as poor ventricular function or diabetes. The additive nature of cardiac risk is illustrated by Siu *et al*[5] who showed that non-lesion specific risk could be estimated from the following risk factors:

- cyanosis ($Sao_2 < 90\%$)
- New York Heart Association (NYHA) symptoms > functional class II
- systemic ventricular ejection fraction < 40%
- prior cardiovascular event (arrhythmia, pulmonary oedema, stroke or transient ischaemic attack).

If one risk factor is present, the additional risk of an adverse cardiac event during pregnancy is 27%. If there are two or more, the risk is 75%.

Conditions in which pregnancy risk is WHO 1 (table 2)

- The risk of maternal morbidity and mortality is not detectably higher than that of the general population.

Conditions in which pregnancy risk is WHO 2 or 3 (table 3)

- WHO 2 conditions carry a small increased risk of maternal mortality or morbidity.
- WHO 3 conditions carry a significant increased risk of maternal morbidity or mortality. These women need expert joint cardiac and obstetric preconception counselling, and care throughout the antenatal and peripartum period.

Individual circumstances dictate whether these patients fall into WHO 2 or WHO 3. The risk is increased if there are additional risk factors or a combination of conditions. For example, the risk of pregnancy in a woman with moderate mitral and aortic regurgitation and mildly impaired left ventricular function will be WHO 3. Similarly the risk of pregnancy would rise from WHO 3 to WHO 4 in a patient with a mechanical valve with left ventricular impairment.

Furthermore, the patient needs to be able to take into account the likely fetal outcome when deciding whether to undertake the risk of pregnancy. This is illustrated in cases of women with cyanotic heart disease (WHO 3 risk), in whom the chance of a live birth is only 12% if the pre-pregnancy resting arterial oxygen saturation (Sao_2) is < 85%.[6]

Table 2 Conditions with WHO 1 pregnancy risk

- Uncomplicated, small or mild
  - pulmonary stenosis
  - ventricular septal defect
  - patent ductus arteriosus
  - mitral valve prolapse with no more than trivial mitral regurgitation
- Successfully repaired simple lesions, e.g.
  - ostium secundum atrial septal defect
  - ventricular septal defect
  - patent ductus arteriosus
  - total anomalous pulmonary venous drainage
- Isolated ventricular extrasystoles and atrial ectopic beats

Conditions in which pregnancy risk is WHO 4 (table 4)

- WHO 4 conditions carry an extremely high risk of maternal mortality or severe morbidity; pregnancy is contraindicated. If pregnancy occurs, termination should be discussed. If pregnancy continues, care as for WHO 3.

Pulmonary arterial hypertension[7 8]

Maternal mortality approaches 50% in women with pulmonary arterial hypertension of any cause.[9] The risk is thought to be due to the presence of fixed high pulmonary vascular resistance resulting in an inability to increase pulmonary blood flow.

Pulmonary arterial hypertension is defined as a non-pregnant elevation of *mean* (not systolic) pulmonary artery pressure ⩾ 25 mm Hg at rest or ⩾ 30 mm Hg on exercise in the absence of a left to right shunt. Mild pulmonary arterial hypertension can also be defined as a pulmonary artery *systolic* pressure ~36–50 mm Hg.

It should be remembered that the risk of maternal death is high even in the presence of mild pulmonary hypertension. In addition, recent UK maternal mortality data suggest that pregnancy may be associated with progression of pulmonary hypertension.[1]

CONTRACEPTION

Both the cardiovascular safety and contraceptive efficacy of each contraceptive method should be considered for each cardiac condition. The method recommended should combine acceptability to the woman with the highest efficacy and safety profile. In contrast to women with normal hearts using contraception to space pregnancies, contraceptive efficacy is paramount for those with serious heart disease in whom pregnancy may be life threatening. The failure rates of different contraceptive methods are shown in table 5.

Barrier methods

The disadvantage of the barrier methods is their user dependency; even in reliable hands, there is a significant

Table 3 Conditions in which pregnancy risk is WHO 2 or 3

WHO 2 if otherwise well and uncomplicated	WHO 2-3 depending on individual	WHO 3
Unoperated atrial septal defect	Mild left ventricular impairment	Mechanical valve
Repaired tetralogy of Fallot	Hypertrophic cardiomyopathy	Systemic right ventricle (e.g. congenitally corrected transposition, simple transposition post Mustard or Senning repair)
Most arrhythmias	Native or tissue valvular heart disease not considered WHO 4	Post Fontan operation
	Marfan syndrome without aortic dilatation	Cyanotic heart disease
	Heart transplantation	Other complex congenital heart disease

failure rate. They are therefore not ideal methods for women in whom a pregnancy must be avoided. However, there are no cardiac contraindications to any barrier methods; indeed the protection they provide against sexually transmitted diseases means that their use as an adjunct to other methods should be encouraged, especially when mutual monogamy cannot be assured.

Combined hormonal contraceptives (CHCs) (table 6)

These preparations contain a combination of estrogen and progestogen. They have a high contraceptive efficacy. In the UK, only the combined oral contraceptive (COC), which is the most popular method, and Evra skin patches are available.

Other estrogen containing preparations not yet licensed in the UK are:

- vaginal ring: NuvaRing
- combined injectable: Cyclofem, Mesigyna, Lunelle.

It is the thrombogenicity of the estrogen component of combined hormonal contraceptives that makes this method unsuitable for many women with heart disease. The risks that apply to the patch, ring and injectables are similar to that of the COC. Estrogen increases the risk of both arterial and venous thrombosis.

Additional risks factors such as smoking, migraine with aura, hypertension, diabetes and obesity further increase the risk of thrombotic events. Anticoagulation with warfarin does not provide complete protection against the thrombotic effects of estrogen. Thus CHCs are WHO 4 (contraindicated) for a woman on warfarin with one of the most thrombogenic mechanical valves such as a single leaflet tilting disc mitral valve, but are WHO 3 (use with caution) for a bileaflet tilting disc aortic valve.

It should be noted that both estrogen and progestogen affect the metabolism of warfarin, so the frequency of international normalised ratio (INR) monitoring should be increased when starting any hormonal contraception.

The presence of an obligatory or potential right to left shunt represents a further risk, since it may permit paradoxical embolism if a venous thrombosis develops. As a result, cyanosis is a contraindication (WHO 4) to CHCs. In addition, women with an unoperated atrial septal defect may intermittently shunt right to left and should be counselled that other methods of contraception may be preferable (WHO 3).

In general, CHCs should be avoided in women in whom the risk of their use is WHO 3. The exceptions are if the woman accepts the risks and rejects the alternatives, or if the risk of pregnancy would be very high and other acceptable contraceptive methods are less effective.

Table 4 Conditions in which pregnancy risk is WHO 4

- Pulmonary arterial hypertension of any cause
- Severe systemic ventricular dysfunction
  - NYHA III–IV or LVEF <30%
- Previous peripartum cardiomyopathy with any residual impairment of left ventricular function
- Severe left heart obstruction
- Marfan syndrome with aorta dilated >40 mm

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Progestogen only methods (table 7)

There is no cardiac contraindication to the use of progestogen; it is not significantly thrombogenic at contraceptive doses.[12–14] However, the progestogen only methods differ in their contraceptive efficacy, side effects and modes of delivery; all these factors must be taken into account when advising on the most appropriate method.

The side effect most likely to be considered unacceptable with progestogen only contraception is menstrual irregularity, but even here there are important differences between methods.

The progestogen only methods available in the UK are:

- Oral preparations
  - progestogen only "minipill"
  - new progestogen only pill: Cerazette
  - emergency contraception: Levonelle

Table 5 Failure rates of different contraceptive methods (adapted from Trussell[10])

	Percentage of women with unintended pregnancy within the first year of use	
Contraceptive method	Typical use	Perfect use
No method	85	85
Barriers	15–32	2–26
Standard POP	5–10	0.5
COC	3–8	0.1
*Cerazette[11]	0.4	0.1
Depo Provera	3	0.3
"Traditional" copper IUD	0.8	0.6
Mirena IUS	0.1	0.1
Implanon	0.05	0.05
Female sterilisation	0.5	0.5
Male sterilisation	0.15	0.15

COC, combined oral contraceptive (estrogen and progestogen); IUD, copper intrauterine device; IUS, levonorgestrel intrauterine system; POP, progestogen-only pill.
*The data on the new POP, Cerazette, are from a different source than the other contraceptive methods in this table and may not therefore be directly comparable. Being from a single study, the Cerazette data are more likely to represent ideal use than typical use. Nonetheless, the efficacy of Cerazette may prove to be greater than both the COC and Depo Provera, because it is taken continuously, without a break, and does not rely on remembering to start a new pack after a week's break or on returning every 12 weeks for a repeat injection.

Table 6 Risk of combined hormonal contraceptives for different cardiac conditions

WHO 1 Always useable	WHO 2 Broadly useable	WHO 3 Caution in use		WHO 4 Do not use	
Minor valve lesions; mitral valve prolapse with trivial mitral regurgitation; bicuspid aortic valve with normal function	Tissue prosthetic valve lacking any WHOs 3 or 4 feature	Thrombotic risk, even on warfarin	Mechanical valves: bileaflet valve	Thrombotic risk, even on warfarin	Mechanical valves: Starr Edwards; Bjork Shiley; any tricuspid valve
Mild pulmonary stenosis			Previous thromboembolism		Ischaemic heart disease
Repaired coarctation with no hypertension or aneurysm	Uncomplicated mild native mitral and aortic valve disease				
Simple congenital lesions successfully repaired in childhood and with no sequelae	Most arrhythmias other than atrial fibrillation or flutter		Atrial arrhythmia		Pulmonary hypertension any cause
	Hypertrophic cardiomyopathy lacking any WHO 3 or 4 features Past cardiomyopathy, fully recovered, including peripartum cardiomyopathy Uncomplicated Marfan syndrome		Dilated left atrium (>4 cm)		Dilated cardiomyopathy and LV dysfunction any cause LVEF <30% Fontan circulation
					Previous arteritis involving coronary arteries, e.g. Kawasaki disease
	Congenital heart disease lacking any WHO 3 or 4 features; small left to right shunt not reversible with physiological manoeuvres, e.g. small VSD	Risk paradoxical embolism	Potential reversal of left to right shunt: unoperated ASD	Risk paradoxical embolism	Cyanotic heart disease; pulmonary AVM

ASD, atrial septal defect; AVM, arteriovenous malformation; LV, left ventricular; LVEF, left ventricular ejection fraction; VSD, ventricular septal defect.

- Long-acting preparations
  - depot injection: Depo Provera
  - intrauterine system (IUS): Mirena
  - subdermal implant: Implanon

Oral preparations

The oral progestogen only preparations tend to cause irregular menstrual bleeding, especially in the first months of use.

- *Progestogen only pill (POP) or "minipill"*—There are no cardiac cautions associated with the minipill, but it is generally not recommended for those with major heart disease in whom pregnancy is high risk (WHO 3 or 4) because of its relatively poor efficacy.
- *Cerazette*—Like the POP, there are no cardiac contraindications to the use of Cerazette. It has the additional advantage of having a contraceptive efficacy akin to that of the COC, because it is anovulatory. It is the pro-drug for the progestogen present in Implanon (see below), so can be used as a trial for the non-bleeding side effects of Implanon. It is a particularly good method for women who wish to use an oral method, but for whom the COC is contraindicated.
- *Levonelle emergency contraception*—There is no cardiac contraindication to this progestogen only "morning after" pill. It has a failure rate of 1% if given within 72 hours of unprotected intercourse. It causes nausea in 15% of women. It potentiates the effects of warfarin; women taking warfarin should have their INR checked within 48 hours of taking Levonelle.

Long-acting preparations

With prolonged use most women become amenorrhoeic, which is an advantage for many women who are cyanotic or anticoagulated, in whom menorrhagia is often a significant problem. This can also be a benefit of Cerazette but is less assured.

- *Depo Provera*—There are no cardiac contraindications to this highly effective contraceptive method. However, its continued efficacy is dependent on regular 12-weekly deep intramuscular injections, since there may be a rapid return to fertility. Haematoma at the site of injection may be a risk in patients anticoagulated with warfarin; in practice this does not appear to be a major problem. Prolonged use is associated with a pronounced fall in estrogen concentrations, and a reduction in bone mineral density. However, bone mass returns to normal within 2–3 years of stopping Depo Provera, and WHO recommends no restrictions to its use with respect to bone health[15].
- *Mirena IUS*—The IUS is an intrauterine device impregnated with levonorgestrel that needs replacing every five years. Its contraceptive efficacy is superior to that of sterilisation. It usually causes advantageous oligoamenorrhoea, in contrast to the menorrhagia and dysmenorrhoea associated with traditional copper coils. Although antibiotic prophylaxis is recommended at the time of insertion, the risk of endocarditis is lower with the IUS than with the copper coil. The cardiovascular risk of the IUS is confined to the time of insertion, in particular to instrumentation of the cervix. The procedure is associated with a vasovagal reaction in up to 5% of women, which may cause potentially fatal cardiovascular collapse in those with a Fontan circulation or pulmonary vascular disease. The risk of such a response may be reduced by the use of a paracervical block or combined spinal and epidural block. In general, therefore, the IUS is not recommended for women with a Fontan circulation of pulmonary vascular disease (WHO 3 risk), and Implanon is to be preferred. However, if Implanon produces

Table 7 Cardiovascular risk of progestogen only contraceptive methods

Method	Cardiac condition	WHO risk
POP minipill	All cardiac patients	1 (But not recommended if pregnancy high risk)
Cerazette	All cardiac patients	1
Levonelle emergency contraception	All cardiac patients	1 (but caution if taking warfarin)
Depo Provera	All cardiac patients	1 3 if taking warfarin
Mirena IUS	Cardiac patients unless:	1
	High endocarditis risk	3
	Pulmonary hypertension, Fontan or other condition where vagal reaction would be poorly tolerated	3
Implanon	All cardiac patients	1

unacceptable menstrual bleeding, then the risk of pregnancy for these patients may outweigh the risk of Mirena insertion by an experienced operator. The IUS can be inserted in nulliparous women, the procedure being best tolerated if performed by a skilled operator. For the majority of women, the risk associated with the IUS is WHO 1 once inserted, and WHO 2 at the time of insertion with antibiotic prophylaxis. For those with a particularly high risk of endocarditis, its use should be considered WHO 3.

- *Implanon*—This subdermal implant is more effective than sterilisation and is effective for three years. There are no cardiac contraindications to its use. It produces less fluctuation in blood concentrations and has fewer hormonally related side effects than Depo Provera. Although it may produce oligoamenorrhoea (20% of women), some women experience prolonged irregular menstrual bleeding necessitating its removal.

Bosentan and hormonal contraception

Women with pulmonary hypertension are among those at highest risk of pregnancy and for whom extremely effective contraception is most important. The endothelin antagonist bosentan is increasingly used in the treatment of pulmonary hypertension. It is an enzyme inducer and significantly reduces the efficacy of some hormonal preparations, so additional protection may be needed (table 8).

Sterilisation

Female sterilisation may seem to the cardiologist to be the logical choice of contraception in a patient in whom pregnancy may be life threatening. However, it may have a major psychological impact, is less effective than Implanon and the IUS, and the procedure itself may carry a significant risk to those women for whom pregnancy is the highest risk. As a result it should be considered WHO 2 at best.

It should also be noted that late failure rates are high in young women,[16 17] and may result in ectopic pregnancy, which places women with heart disease at high risk. The failure rate is also higher when performed at the time of caesarean section.[16]

Laparoscopic sterilisation requires insufflation of the abdomen with carbon dioxide, intermittent head down tilt and positive pressure ventilation, all of which combine to reduce cardiac output and may be poorly tolerated by those with a Fontan circulation or pulmonary vascular disease. There is also a risk of air embolism, which may be paradoxical in those with a right to left shunt. The safest surgical technique in skilled hands is probably a mini-laparotomy with combined spinal and epidural anaesthesia.

Essure is a new stent based sterilisation technique, inserted hysteroscopically into the Fallopian tubes, with sedation and local anaesthesia. Early studies suggest it is irreversible, with a very low failure rate.[18 19]

Vasectomy is rarely appropriate since it assumes monogamy, and the male partner may outlive his female partner with heart disease and wish to have a family with a new partner.

Risks of contraception and pregnancy in heart disease: key points

- Cardiac disease is a leading cause of maternal death in the UK
- For women with heart disease:
  - pregnancy may be life threatening
  - there is a safe and effective method of contraception for each condition
- Cardiologists need to:
  - understand the risks of pregnancy in women with heart disease
  - appreciate the need to refer high risk women for specialist pre-pregnancy counselling and antenatal care
  - offer appropriate contraceptive advice

Table 8 Effects of bosentan on efficacy of progestogen contraception

Contraceptive method	Effect of bosentan on contraceptive efficacy	Recommendation for use in women with pulmonary vascular disease taking bosentan
POP (''minipill'')	Reduced	WHO 4, do not use
Cerazette	Reduced	WHO 2 if double dose taken
Levonelle	Reduced	WHO 2 if double dose taken
Depo Provera	No effect	WHO 1, no contraindication
Mirena IUS	No effect	WHO 3, because of risk of vagal reaction at insertion in pulmonary hypertension
Implanon	Reduced	WHO 2 if additional daily Cerazette taken

CONCLUSION

The number of women of childbearing age with congenital or acquired heart disease is increasing. Reflecting this change, maternal deaths from cardiac disease in the UK have increased steadily over the last decade. If this trend is to be reversed, cardiologists need to develop the skills to broach the subjects of pregnancy and contraception, and to give appropriate advice or to make a specialist referral.

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APPENDIX

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